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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/477,082	12/30/1999	VINCENT J. KIDD	2427/IE988-U	8684

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EXAMINER

HOLLERAN, ANNE L

ART UNIT	PAPER NUMBER
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1642

DATE MAILED: 07/08/2003

22

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Applicati n No.

09/477,082

Applicant(s)

KIDD ET AL.

Examiner

Anne Holleran

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12/4/2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 2,3,11-16,27-29,48-51 and 54-62 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

- 5) ☐ Claim(s) _____ is/are allowed.

- 6) ☒ Claim(s) 2,3,11-16,27-29,48-51 and 54-61 is/are rejected.

- 7) ☒ Claim(s) 61 and 62 is/are objected to.

- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☒ Interview Summary (PTO-413) Paper No(s). 21.
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____. 6) ☐ Other: _____

DETAILED ACTION

1. The finality of the previous Office action is withdrawn in view of the new art rejections.
2. The amendment filed Dec. 4, 2002 (Paper No. 20) is acknowledged. Claims 4-9, 17-25, 30-47 and 52-53 were canceled. Claims 58-62 were added.

Claims 2, 3, 11-16, 27-29, 48-51, 54-62 are pending and examined on the merits.

Claim Rejections Withdrawn:

3. The rejection of claims 11-20 and 51-54 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for the recitation of "poor prognosis" is withdrawn in view of the amendment canceling claims 17-20, 52 and 53, and amending claims, 13-16, 51 and 54.
4. The rejection of claims 2-9, 11-20, 27-29, and 48-57 under 112 second paragraph for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for the newly added recitation of "reduction in the total level of expression of CASP8 protein to below that necessary for proper cellular regulation" is withdrawn in view of the amendment canceling claims 4-9, 17-20, and 52-53, and amending claims 2, 3, 13-16, 27-29, 48-51 and 54-57.

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New Grounds of Rejection:

5. Claims 55 and 27-29, 58 and 59 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 55 is indefinite because it is drawn to a kit, but is set forth as comprising an “assay”, which is usually defined as a set of methods steps. Thus, the scope of claim 55 is unclear because it is not clear if a product or a method is being claimed.

6. Claims 2, 3, 48, 49, 50, 27-28, 54, 55, and 56 are rejected under 35 U.S.C. 102(e) as being anticipated by Hunter (US Patent 6,172,190; January 9, 2001; effective filing date Feb. 27, 1997).

Claims 2, 3, 48, 49, 50, 54, and 56 are drawn to methods for detecting inactivation of CASP8 gene expression. The methods may comprise the steps of detecting the absence of expression of a CASP8 protein, or the methylation of CASP8 genomic DNA, or the absence of CASP8 mRNA. Claims 55, 27 and 28 are drawn to kits for the detection of CASP8 inactivation, comprising an assay for detecting methylation of CASP8 genomic DNA, where the assay may comprise a PCR assay or oligonucleotide PCR primers for amplification of at least part of CASP8 genomic DNA. Kits are interpreted as product claims with an intended use preamble that does not affect the scope of the product contained within the kit.

It is noted that the specification fails to define the term CASP8. Therefore, given its broadest reasonable interpretation, CASP8 is interpreted to encompass any of the genes encoding any of the caspase-8 variants.

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Hunter teaches methods comprising detecting the absence of Caspase-8h or Caspase-8i proteins, where the detection is by immunoassay or biochemical assay of caspase-8h or caspase-8i protein (see col. 21, lines 4-6, col. 22, line 8- col. 23, line 56), where the detection is of caspase-8h or caspase-8i mRNA (see col. 21, line 56- col. 22, line 6), or where the detection is of caspase-8h or caspase-8i methylation by RNase protection assay (see col. 30, lines 58-65). Hunter also teaches PCR primers for use in PCR assays (see col. 13, line 2-10, col. 13, line 51 – col. 14, line 5). Thus, Hunter teaches the claimed methods and kits.

7. Claims 2, 3, 11-15, 27, 28, 48-51, and 54-56 are rejected under 35 U.S.C. 102(b) as being anticipated by Dixit (WO 97/46662; published 11 Dec. 1997).

Claims 2, 3, 48, 49, 50, 54, and 56 are drawn to methods for detecting inactivation of CASP8 gene expression. The methods may comprise the steps of detecting the absence of expression of a CASP8 protein, or detecting the methylation of CASP8 genomic DNA, or detecting the absence of CASP8 mRNA. Claims 55, 27 and 28 are drawn to kits for the detection of CASP8 inactivation, comprising an assay for detecting methylation of CASP8 genomic DNA, where the assay may comprise a PCR assay or oligonucleotide PCR primers for amplification of at least part of CASP8 genomic DNA. Kits are interpreted as product claims with an intended use preamble that does not affect the scope of the product contained within the kit. Claims 11-15 and 51 are drawn to methods for diagnosis or prognosis of a cancer comprising detecting inactivation of a CASP8 gene expression, where the methods may comprise the steps of detecting the absence of expression of a CASP8 protein, or the methylation of CASP8 genomic DNA, or the absence of CASP8 mRNA. Claims 11-15 and 51 fail to relate

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the method steps to the purpose stated in the preamble, and therefore are interpreted as reading on methods that comprise steps of detecting the absence of expression of a CASP8 protein, or the methylation of CASP8 genomic DNA, or the absence of CASP8 mRNA.

Dixit teaches methods of detection of "apoptosis protease-7", which is also known as ICE LAP-7 or FLICE, which is another name for caspase-8. Dixit teaches assays of caspase-8 that comprise detecting the absence of CASP8 protein (see page 52, line 2- page 53, line4), that comprise detecting the absence of CASP8 mRNA (page 45, lines 1-18; page 48, lines 14-31), that comprise detecting methylation of CASP8 genomic DNA (by RNase protection assay, page 48, lines 14-18). Dixit also teaches PCR primers for use in PCR assays (page 47, lines 5-19). Thus, Dixit teaches methods and kits that are the same as that claimed.

8. Claims 27, 28 and 55 are rejected under 35 U.S.C. 102(b) as being anticipated by Wallach (WO 97/03998; published 6 Feb. 1997).

Claims 55, 27, 28 are drawn to kits comprising oligonucleotide primers for amplification of at least part of CASP8 genomic DNA. Kits are interpreted as product claims with an intended use preamble that does not affect the scope of the product contained within the kit.

Wallach teaches oligonucleotide primers for PCR detection of MACH proteins (MACH is another name for caspase-8; see page 81, line 8- page 82, line 9). Thus, Wallach teaches kits that are the same as that claimed.

9. Claims 27, 28 and 55 are rejected under 35 U.S.C. 102(b) as being anticipated by Alnemri (WO 97/35020; published 25 Sep. 1997).

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Claims 55, 27, 28 are drawn to kits comprising oligonucleotide primers for amplification of at least part of CASP8 genomic DNA. Kits are interpreted as product claims with an intended use preamble that does not affect the scope of the product contained within the kit.

Alnemri teaches oligonucleotide primers for PCR detection of an Mch5 protein (MchR is another name for caspase-8; see page 55, lines 1-19). Thus, Alnemri teaches kits that are the same as that claimed.

10. Claims 2, 3, 11-14, 48 and 51 are rejected under 35 U.S.C. 102(b) as being anticipated by Scaffidi (Scaffidi, C. et al, Journal of Biol. Chem., 272(43): 26953-26958, 1997, Oct.).

Claims 2, 3, 11-14, 48 and 51 are drawn to methods comprising the detection of the absence of CASP8 protein. CASP8 protein is interpreted broadly to encompass any of the caspase-8 protein isoforms.

Scaffidi teaches the detection of the absence of caspase-8 protein (see page 26954, 2nd col., bridging para to page 26955, 1 col., 2nd paragraph). Thus, Scaffidi teaches the methods as claimed.

11. Claims 2, 3, 11-14, 48 and 51 are rejected under 35 U.S.C. 102(a) as being anticipated by Juo (Juo, P. et al, Current Biol., 8: 1001-1008, 1998, Sep.).

Juo teaches the detection of the absence of caspase-8 protein (see page 1002, 1st col.-2nd col.; page 1006, 1st col., - page 1007, 1st col.). Thus, Juo teaches methods that are the same as that claimed.

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12. Claims 15, 16, 27-29, 55-57 and 60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dixit (WO 97/46662; published 11 Dec. 1997) in view of Herman I (Herman, J.G. et al, Proc. Natl. Acad. Sci., USA, 91: 9700-9704, 1994) and further in view of Herman II (Herman, J. G. et al, Proc. Natl. Acad. Sci., USA, 93: 9821-9826, 1996).

Claims 56, 57 and 60 are drawn to methods for detecting inactivation of CASP8 gene expression, comprising the detection of methylation of CASP8 genomic DNA, where methylation occurs in the 5'-untranslated region. Claims 55, and 27-20 are drawn to kits for the detection of CASP8 inactivation, comprising an assay for detecting methylation of CASP8 genomic DNA, where the assay may comprise a PCR assay or oligonucleotide PCR primers for amplification of at least part of the 5'-untranslated region of CASP8 genomic DNA. Kits are interpreted as product claims with an intended use preamble that does not affect the scope of the product contained within the kit. Claims 15 and 16 are drawn to methods for diagnosis or prognosis of a cancer comprising detecting inactivation of a CASP8 gene expression, where the methods the methylation of CASP8 genomic DNA. Claims 15 and 16 fail to relate the method steps to the purpose stated in the preamble, and therefore are interpreted as reading on methods that comprise steps of detecting the methylation of CASP8 genomic DNA in the 5'-untranslated region of CASP8 genomic DNA.

Dixit teaches methods of detection of "apoptosis protease-7", which is also known as ICE LAP-7 or FLICE, which is another name for caspase-8. Dixit teaches assays of caspase-8 that comprise detecting methylation of CASP8 genomic DNA (by RNase protection assay, page 48, lines 14-18). Dixit also teaches PCR primers for use in PCR assays (page 47, lines 5-19).

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Dixit fails to teach or suggest method for detection of methylation in the 5'-untranslated region of caspase-8 genomic DNA.

However, Herman I teaches that alteration of DNA methylation is recognized as a consistent molecular change in human tumors, and the regions of hypermethylation usually occur in CpG islands found in and around the 5' regulatory areas of genes. Herman I also teaches that aberrant methylation of CpG islands of tumor suppressor genes may provide a mechanism for inactivation of tumor suppressor genes during tumor progression (see page 9700, 1st col).

Herman II teaches a PCR assay method for the detection of methylation status or CpG islands (see page 9821, 1st col., and 2nd col, last para.; page 9822, 1st – 2nd col., bridging para.). Dixit teaches that alterations of caspase-8 (FLICE) expression is associated with disease such as tumorigenesis (see page 45, lines 1-18; and page 46, lines 18-25; page 48, lines 14-31), because caspase-8 plays a role in apoptosis (page 8, line 3 – page 9, line 15).

Thus, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have modified the methods or kits of Dixit to make the claimed methods or kits, where the combination of teachings of Dixit and Herman II resulted in methods and kits useful for the detection of methylation in the 5'-untranslated region of the caspase-8 gene. One would have been motivated to modify the methods and kits of Dixit, because of the teachings of Herman I, directing one to detect hypermethylation in the 5'-untranslated regions of genes, where lack of expression is associated with cancer.

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Conclusion


No claim is allowed. Claims 61 and 62 are objected to for depending from rejected claims. Claims 2, 3, 11-16, 27-29, 48-51, 54-60 are rejected.

Any inquiry concerning this communication or earlier communications from the Office should be directed to Anne Holleran, Ph.D. whose telephone number is (703) 308-8892. Examiner Holleran can normally be reached Monday through Friday, 9:30 am to 2:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D. can be reached at (703) 308-3995.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist at telephone number (703) 308-0196.

Anne L. Holleran
Patent Examiner
July 3, 2003


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